

WE CLAIM:

1. An core/shell nanoparticle comprising:
 - (a) an inner metal-containing nanoparticle core; and
 - (b) an outer non-alloying gold shell surrounding the nanoparticle core.
- 5
2. A core/shell nanoparticle specific binding substance conjugate comprising:
 - (a) an inner metal-containing nanoparticle core;
 - (b) an outer non-alloying gold shell surrounding the nanoparticle core; and
 - (c) specific binding substance attached to the gold shell.
- 10
3. A core/shell nanoparticle oligonucleotide conjugate comprising:
 - (a) an inner metal-containing nanoparticle core;
 - (b) an outer non-alloying gold shell surrounding the nanoparticle core; and
 - (c) oligonucleotides attached to the gold shell.
- 15
4. The core/shell nanoparticle of claim 3 wherein the oligonucleotides have a sequence complementary to a portion of a sequence of a target nucleic acid.
- 20
5. The core/shell nanoparticle of claims 1, 2 or 3 wherein the inner metal-containing nanoparticle core comprises silver, Pt, Fe, Co, or Ni.
- 25
6. The core/shell nanoparticle of claims 1, 2 or 3 wherein the inner metallic nanoparticle core comprises an alloy metal comprising FePt or FeAu.
7. The core/shell nanoparticle of claims 1, 2 or 3 wherein the inner metal-containing nanoparticle core comprises a metal oxide.
- 30
8. The core/shell nanoparticle of claims 1, 2 or 3 wherein the inner metal-containing nanoparticle core is magnetic.
9. The core/shell nanoparticle of claim 7 wherein the inner metal-containing nanoparticle core comprises Fe_3O_4 or Co_3O_4 .

10. The core/shell nanoparticle of claims 1, 2 or 3 wherein the gold shell ranges from about 0.5 to about 2 monolayers in thickness.

5 11. The core/shell nanoparticle of claim 3 wherein the oligonucleotides are attached to the nanoparticles in a stepwise ageing process comprising (i) contacting the oligonucleotides with the nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles; (ii) adding at least one salt to the aqueous solution to create a second aqueous solution; and (iii) contacting 10 the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles;

15 12. The method of Claim 11 wherein the oligonucleotides include a moiety comprising a functional group which can bind to a nanoparticle.

13. The method of Claim 11 wherein all of the salt is added to the water in a single addition.

20 14. The method of Claim 11 wherein the salt is added gradually over time.

25 15. The method of Claim 11 wherein the salt is selected from the group consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, a combination of two or more of these salts, one of these salts in a phosphate buffer, and a combination of two or more these salts in a phosphate buffer.

16. The method of Claim 15 wherein the salt is sodium chloride in a phosphate buffer.

30 17. The method of Claim 11 wherein nanoparticle-oligonucleotide conjugates are produced which have the oligonucleotides present on surface of the nanoparticles at a surface density of at least 10 picomoles/cm².

18. The method of Claim 17 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm².

19. The method of Claim 18 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm² to about 40 picomoles/cm².
5

20. A nanostructure comprising the core/shell nanoparticles of claims 1 or 2.

10 21. A silver/gold core/shell nanoparticle comprising:
(a) an inner silver nanoparticle core; and
(b) an outer non-alloying gold shell surrounding the nanoparticle core.

15 22. A magnetic core/shell nanoparticle comprising:
(a) an inner Fe₃O₄ nanoparticle core; and
(b) an outer non-alloying gold shell surrounding the nanoparticle core.

23. The core/shell nanoparticle oligonucleotide conjugate of any of claims 2 or 3 exhibiting a surface plasmon absorption peak at about 500 to 530 nm.
20

24. A method for preparing core/shell nanoparticles comprising the steps of:
(a) providing inner metal-containing nanoparticle cores;
(b) treating the inner metal-containing nanoparticle cores simultaneously with a solution comprising a gold salt and a solution comprising a reducing silverent at 0 °C to produce a non-alloying gold shell surrounding the nanoparticle cores; and
(c) isolating the core/shell nanoparticles.
25

26. The method according to claim 24 wherein the gold salt comprises HAuCl₄, NaAuCl₄, KAuCl₄, or KAu(CN)₂.
30

26

27. The method according to claim 24 wherein the reducing silverent comprises NaBH₄ or ascorbic acid.

28. The method according to claim 27 wherein the reducing silverent comprises
5 NaBH₄.

29. The method according to claim 24 wherein the gold salt and reducing silverent are present at a ratio ranging from about 1:2 to about 1:20.

10 30. A product produced by the method of 24.

31. The product of claim 30 wherein the gold shell thickness is about 0.15 to 0.6
nm.

15 32. A method of detecting nucleic acid bound to a surface comprising:

(a) contacting the surface with a solution comprising core/shell nanoparticle oligonucleotide conjugates of claim 2, wherein the contacting takes place under conditions effective to allow hybridization of the core/shell nanoparticle oligonucleotide conjugates with the bound nucleic acid;

(b) subjecting the nanoparticle conjugate to an external magnetic field so as to accelerate movement of the nanoparticle conjugate to the surface to promote interaction between the nanoparticle conjugate and the nucleic acid;

(c) removing from the surface any nanoparticle conjugates that have not hybridized with the nucleic acid; and

(d) observing a detectable change brought about by hybridization of the nucleic acid with the nanoparticle conjugates.

33. The method of claim 32 wherein the core/shell nanoparticle oligonucleotide conjugate comprises Fe₃O₄/gold core/shell nanoparticles.

30 34. The method of claim 32 wherein step (c) is performed by rinsing the surface with a wash solution or reversing the magnetic field.

35. A method of detecting a target analyte bound to a surface comprising:

- (a) providing a surface that includes a bound target analyte;
- (b) contacting the surface with a solution comprising core/shell nanoparticle receptor conjugate, wherein the receptor specifically binds to the analyte, wherein the contacting takes place under conditions effective to allow binding of the nanoparticle conjugates with the bound nucleic acid;
- (c) subjecting the nanoparticle conjugate to an external magnetic field so as to accelerate movement of the nanoparticle conjugate to the surface to promote binding interaction between the nanoparticle conjugate and the target analyte;
- (d) removing from the surface any nanoparticle conjugates that have not bound with the target analyte; and
- (e) observing a detectable change brought about by binding interaction of the target analyte with the nanoparticle conjugates.